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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/373,658	08/13/99	IRUELA-ARISPE L	1448.1070006

HM12/0510
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EXAMINER	
CANELLA,K	
ART UNIT	**PAPER NUMBER**
1642	

DATE MAILED: 05/10/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
09/373,658	Iruela-Arispe et al
Examiner	**Group Art Unit**
Karen Canella	1642

☐ Responsive to communication(s) filed on _____

☐ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *3 months* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claim

☒ Claim(s) *24-85* is/are pending in the applicat

Of the above, claim(s) _____ is/are withdrawn from consideration

☒ Claim(s) *57-66* is/are allowed.

☒ Claim(s) *24-56 and 67-85* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☒ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____ .

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). *5,8*

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

1. Acknowledgment is made of applicants election with traverse of Group I, drawn to polynucleotides of SEQ ID NO:1 and SEQ ID NO:125 and polynucleotides encoding SEQ ID NO:2 and SEQ ID NO:126. The traversal is on the grounds that the examiner has failed to show that the examination of elected Group I along with Group II, drawn to METH1 polypeptides, would entail a serious burden of search. This has been considered but not found persuasive as burden of search is not the sole requirement for restriction between inventions that are patentably distinct. The polynucleotide of Groups I and the polypeptides of Group III represent distinct products having widely differing properties, methods of making and functions. Furthermore, as Groups I and III are classified differently, an examination of both groups would require different searches in the U.S. Patent Shoes and the scientific literature and would require the consideration of different patentability issues. Because these products are distinct for the reasons given above and because the searches required for the products are not co-extensive, restriction for examination purposes is considered proper. For these reasons the restriction requirement is deemed to be proper and is adhered to. The requirement is therefore made FINAL.

2. Amendments to the specification, as requested in Paper No. 10, filed 11/6/2000, have not been entered as there is no references to SEQ ID NO:125 on page 102 or 153 of the instant specification.

3. Claims 1-23 have been canceled. Claims 24-85 have been added and are examined on the merits

Claim Rejections - 35 USC § 112

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 24-56 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claims 24 and 46 are vague and indefinite in the reference to SEQ ID NO:126 as a polypeptide as SEQ ID NO:126 is a polynucleotide of 4014 nucleotides in the CRF. Claims 25, 26, 38 and 47-49 are vague and indefinite in the reference to SEQ ID NO:125 as a polynucleotide as SEQ ID NO:125 is a polypeptide of 968 amino acid residues in the CRF. For purpose of examination, claims 24 and 46 will be read as being drawn to the polypeptide of SEQ ID NO:125, and claims 25, 26, 38 and 47-49 will be read as being drawn to the polynucleotide of SEQ ID NO:126.

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 38-56 and 67-85 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for polynucleotides comprising SEQ ID NO:1 and 126 and polynucleotides encoding SEQ ID NO:2 and 125 as well as polynucleotides fully complementary to polynucleotides comprising SEQ ID NO:1 and 126 and polynucleotides which are fully complementary to the polynucleotides encoding SEQ ID NO:2 and 125, does not reasonably provide enablement for polynucleotides which hybridize to SEQ ID NO:1 or SEQ ID NO:126, or polynucleotides which are less than fully complementary to SEQ ID NO:1 or SEQ ID NO:126, or polynucleotides which are less than fully complementary to the polynucleotides encoding SEQ ID NO:2 or SEQ ID NO:125, or polynucleotides which are at least 95% identical to

polynucleotides comprising SEQ ID NO:1 or SEQ ID NO:126. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

(A) As drawn to polynucleotide variants

Claims 48-56 and 77-85 are drawn to polynucleotides comprising nucleic acid sequences which are at least 95% identical to SEQ ID NO:126 or SEQ ID NO:1, vectors and host cells thereof, and methods of expressing recombinant proteins. The specification teaches the recombinant expression of polynucleotides of SEQ ID NO:126 or SEQ ID NO:1 results in proteins which have angiogenesis inhibiting activity. One cannot extrapolate the teaching of the specification to the scope of the claims because, when given the broadest reasonable interpretation, the claims are clearly intended to encompass species of polynucleotides that encode proteins and peptides having neither structural nor functional identity with polynucleotides encoding METH1 and no guidance has been given as to how to use these species. Further, the specification has not shown that polynucleotides comprising variants of SEQ ID NO:1 or 126 are capable of functioning as that which is suggested. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with the claims since the specification gives no guidance on, or exemplification of, how to make/use the polynucleotides that encode functional angiogenesis inhibitors beyond the polynucleotides which encode SEQ ID NO:2 or SEQ ID NO:125. Protein chemistry is probably one of the most unpredictable areas of biotechnology and it cannot be anticipated that a single amino acid substitution will not alter the activity of a polypeptide. For example, as disclosed by Burgess et al (J of Cell Bio. 111:2129-2138, 1990), replacement of a single lysine reside at position 118 of acidic fibroblast growth factor by glutamic acid led to the substantial loss of heparin binding, receptor binding and biological activity of the protein. In transforming growth factor alpha, replacement of aspartic acid at position 47 with alanine or asparagine did not affect biological activity while replacement with serine or glutamic acid sharply

reduced the biological activity of the mitogen. (Lazar et al. Molecular and Cellular Biology 8:1247-1252 (1988)). These references demonstrate that even a single amino acid substitution or what appears to be an inconsequential chemical modification will often dramatically affect the biological activity and characteristic of a protein. Clearly, it could not be predicted that a polynucleotide comprising a variant polynucleotide having 95% identity to SEQ ID NO:1 or SEQ ID NO:126 would even be a member of the METH family. Reasonable correlation must exist between the scope of the claims and scope of enablement set forth, and it cannot be predicted from the disclosure how to make/use polynucleotides, comprising variants of SEQ ID NO:1 or SEQ ID NO:126. In view of the above, one of skill in the art would be forced into undue experimentation in order to practice the broadly claimed inventions.

(B)As drawn to polynucleotides which hybridize to SEQ ID NO:1 and SEQ ID NO:126, and polynucleotides which are less than fully complementary to disclosed polynucleotides.

Claims 38-45 and 69-76 are drawn to polynucleotides which hybridize under stringent conditions to a probe consisting of nucleotides 466 to 3366 of SEQ ID NO:126 and a probe consisting of nucleotides 1-2853 of SEQ ID NO:1, vectors and host cells comprising the hybridizing polynucleotides and methods of producing recombinant protein. Claims 46, 47, 67 and 68 are drawn to polynucleotides which are complementary to polynucleotides encoding SEQ ID NO:2 and SEQ ID NO:125 and as such encompass polynucleotides which are complementary to fragments of the polynucleotides encoding SEQ ID NO:2 or SEQ ID NO:125. Furthermore, the recitation of hybridization conditions is not limiting, as a smaller oligomer could hybridize under stringent conditions to the probes, as well as lengthy polynucleotides having single base mismatches within regions of homology. For the reasons given in the above paragraph, it would be expected that a substantial number of the hybridizing or complementary polynucleotides encompassed by the claims would not share either structural or functional properties with polynucleotides that encode METH1 or encode proteins that have angiogenesis inhibiting properties. The specification fails to provide an enabling disclosure for how one would use such

polynucleotides. When given the broadest reasonable interpretation, the claims are clearly intended to encompass a variety of species including full-length cDNAs, genes and protein coding regions having no relation to polynucleotides which encode METH1. The specification provides insufficient guidance with regard to these issues and provides no working examples which would provide guidance to one skilled in the art on how to use the broadly claimed species. For the above reasons, undue experimentation would be required to practice the claimed invention.

8. Claims 38-56 and 67-85 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The written description in this case only sets forth SEQ ID NO:1, 126 and polynucleotides encoding SEQ ID NO:2 and 125 and therefore the written description is not commensurate in scope with the claims drawn to polynucleotide variants having at least 95% identity to SEQ ID NO:1 and SEQ ID NO:126, isolated polynucleotides which hybridize under stringent conditions to SEQ ID NO:1 and SEQ ID NO:126, or isolated polynucleotides comprising polynucleotides which are less than fully complementary to SEQ ID NO:1 and 126 or the polynucleotides encoding SEQ ID NO:2 and 125.

Vas-Cath Inc. V. Mahurkar, 19 USPQ2d 1111, clearly states that applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the written description inquiry, whatever is now claimed. (See page 1117). The specification does not clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed. (See Vas-Cath at page 1116).

Applicant is reminded that Vas-Cath makes clear that the written description provision of 35 USC 112 is severable from its enablement provision (see page 115).

For the reason states in paragraph 6 (A and B) supra, with the exception of SEQ ID NO:1 or SEQ ID NO:126 or the polynucleotides encoding SEQ ID NO:2 or SEQ ID NO:125 or polynucleotides which are fully complementary to SEQ ID NO:1 or SEQ ID NO:126 or polynucleotides which are fully complementary to the polynucleotides encoding SEQ ID NO:2 or SEQ ID NO:125, the skilled artisan cannot envision the detailed structure of the encompassed polynucleotides and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and a reference to a potential method of isolating it. The nucleic acid itself is required. See Fiers v. Revel, 25 USPQ 2d 1601 at 1606 (CAFC 1993) and Amgen Inc. V. Chugai Pharmaceutical Co. Lts., 18 USPQ2d 1016.

Furthermore, In The Regents of the University of California v. Eli Lilly (43 USPQ2d 1398-1412), the court held that a generic statement which defines a genus of nucleic acids by only their functional activity does not provide an adequate written description of the genus. The court indicated that while Applicants are not required to disclose every species encompassed by a genus, the description of a genus is achieved by the recitation of a representative number of DNA molecules, usually defined by a nucleotide sequence, falling within the scope of the claimed genus. At section B(1), the court states that an adequate written description of a DNA requires a precise definition, such as by structure, formula, chemical name, or physical properties, not a mere wish or plan for obtaining the claimed chemical invention.

As the instant specification fails to support the generic claims as provided by the Interim Written Description Guidelines published in the June 15, 1998 Federal Register at Volume 63, Number 114, pages 32639-32645., only an isolated DNA molecules comprising SEQ ID NO:1, SEQ ID NO:126, nucleotides 1-2853 of SEQ ID NO:1, nucleotides 466-3366 of SEQ ID NO:126, polynucleotides encoding SEQ ID NO:2, SEQ ID NO:125, amino acid residues 1-950 of

SEQ ID NO:2, amino acid residues 1-967 of SEQ ID NO:125, but not the full breadth of the claims meets the written description provision of 35 USC 112, first paragraph.

Conclusion

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Karen Canella whose telephone number is (703) 308-8362. The examiner can normally be reached on Monday through Friday from 8:30 am to 6:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa, can be reached on (703) 308-3995. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Karen A. Canella, Ph.D.
Patent Examiner, Group 1642
May 4, 2001

GEETHA P. BANSAL
PRIMARY EXAMINER